Refine Search

Search Results -

Term	Documents
ASSAY	224216
ASSAYS	149584
(32 AND ASSAY).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	4
(L32 AND ASSAY).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	4

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L33

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Thursday, February 09, 2006 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L33	L32 and assay	4	L33
L32	L31 and inhibitor	17	L32
L31	L30 and @py<2000	45	L31
L30	L29 and obesity	2246	L30
L29	PPAR	5285	L29
L28	L27 and obesity	0	L28
L27	L26 and @py<2000	17	L27
L26	L25 and compound	393	L26

L25	L24 and binding	396	L25
L24	L23 and assay	396	L24
L23	L22 and in vitro	398	L23
L22	L21 and identify	804	L22
L21	L20 and method	1615	L21
L20	L19 and inhibitor	1642	L20
L19	L18 and ligand	2142	L19
L18	PPAR	5285	L18
L17	L10 and @py<2000	1	L17
L16	L11 and @py<2000	0	L16
L15	L14 and in vitro	180	L15
L14	L9 and py<2000	366	L14
L13	L12 and @py<2000	0	L13
L12	L10 and in vitro	155	L12
L11	L10 and in vitro	155	L11
L10	L9 and treat	298	L10
L9	L8 and obesity	366	L9
L8	L7 and identify	608	L8
L7	L6 and assay	935	L7
L6	L5 and method	998	L6
L5	L3 and inhibitor	998	L5
L4	L2 and beta	2520	L4
L3	L2 and sigma	1111	L3
L2	PPAR	5285	L2
L1	PPAR sigma	0	L1

END OF SEARCH HISTORY

FILE 'WPIDS' ENTERED AT 08:56:44 ON 09 FEB 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'WPIFV' ENTERED AT 08:56:44 ON 09 FEB 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s PPAR sigma and inhibitor and assay
  15 FILES SEARCHED...
  27 FILES SEARCHED...
  48 FILES SEARCHED...
L1   0 PPAR SIGMA AND INHIBITOR AND ASSAY

=> s PPAR sigma
  32 FILES SEARCHED...
L2   14 PPAR SIGMA

=> dup rem
ENTER L# LIST OR (END):L2
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2,
FEDRIP, FOREGE, GENBANK, IMSPRODUCT, IMSRESEARCH, KOSMET, NUTRACEUT, PCTGEN,
PHAR, PHARMAML, PROUSDDR, PS, RDISCLOSURE, SYNTHLINE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L2
L3   14 DUP REM L2 (0 DUPLICATES REMOVED)

=> s L2 and inhibitor
  36 FILES SEARCHED...
L4   4 L2 AND INHIBITOR

=> s L4 and assay
  41 FILES SEARCHED...
L5   0 L4 AND ASSAY

=> d L4 ibib,abs

L4   ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:149965 BIOSIS
DOCUMENT NUMBER: PREV200200149965
TITLE: Prostacyclin-dependent apoptosis mediated by PPARdelta.
AUTHOR(S):   Hatae, Toshihisa; Wada, Masayuki; Yokoyama, Chieko;
                    Shimonishi, Manabu; Tanabe, Tadashi [Reprint author]
CORPORATE SOURCE: Department of Pharmacology, National Cardiovascular Center
                    Research Institute, Fujishiro-dai, Suita, Osaka, 565-8565,
                    Japan
                    tanabe@jsc.ri.ncvc.go.jp
SOURCE: Journal of Biological Chemistry, (December 7, 2001) Vol.
                    276, No. 49, pp. 46260-46267. print.
                    CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
                    Last Updated on STN: 26 Feb 2002
AB   Prostacyclin (PGI2) plays important roles in hemostasis both as a
     vasodilator and an endogenous **inhibitor** of platelet aggregation.
     PGI2 functions in these roles through a specific IP receptor, a G
     protein-coupled receptor linked to Gs and increases in cAMP. Here, we
     report that intracellular prostacyclin formed by expressing prostacyclin
     synthase in human embryonic kidney 293 cells promotes apoptosis by
     activating endogenous peroxisome proliferator-activated receptor delta
     (PPARdelta). In contrast, treatment of cells with extracellular
     prostacyclin or dibutyryl cAMP actually reduced apoptosis. On the
     contrary, treatment of the cells with RpcAMP (adenosine 3',5'-cyclic
     monophosphothioate, Rp-isomer), an antagonist of cAMP, enhanced
     prostacyclin-mediated apoptosis. The expression of an L431A/G434A mutant
     of PPARdelta completely blocked prostacyclin-mediated PPARdelta activation

and apoptosis. These observations indicate that prostacyclin can act through endogenous PPARdelta as a second signaling pathway that controls cell fate.

=> d L4 1-4 ibib,abs

L4 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:149965 BIOSIS
DOCUMENT NUMBER: PREV200200149965
TITLE: Prostacyclin-dependent apoptosis mediated by PPARdelta.
AUTHOR(S): Hatae, Toshihisa; Wada, Masayuki; Yokoyama, Chieko; Shimonishi, Manabu; Tanabe, Tadashi [Reprint author]
CORPORATE SOURCE: Department of Pharmacology, National Cardiovascular Center Research Institute, Fujishiro-dai, Suita, Osaka, 565-8565, Japan
tanabe@jsc.ri.ncvc.go.jp
SOURCE: Journal of Biological Chemistry, (December 7, 2001) Vol. 276, No. 49, pp. 46260-46267. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002

AB Prostacyclin (PGI2) plays important roles in hemostasis both as a vasodilator and an endogenous **inhibitor** of platelet aggregation. PGI2 functions in these roles through a specific IP receptor, a G protein-coupled receptor linked to Gs and increases in cAMP. Here, we report that intracellular prostacyclin formed by expressing prostacyclin synthase in human embryonic kidney 293 cells promotes apoptosis by activating endogenous peroxisome proliferator-activated receptor delta (PPARdelta). In contrast, treatment of cells with extracellular prostacyclin or dibutyryl cAMP actually reduced apoptosis. On the contrary, treatment of the cells with RpcAMP (adenosine 3',5'-cyclic monophosphothioate, Rp-isomer), an antagonist of cAMP, enhanced prostacyclin-mediated apoptosis. The expression of an L431A/G434A mutant of PPARdelta completely blocked prostacyclin-mediated PPARdelta activation and apoptosis. These observations indicate that prostacyclin can act through endogenous PPARdelta as a second signaling pathway that controls cell fate.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1262399 CAPLUS
DOCUMENT NUMBER: 144:22712
TITLE: Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Epple, Robert; Azimioara, Mihai
PATENT ASSIGNEE(S): Irm LLC, Bermuda
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113506	A1	20051201	WO 2005-US16747	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-571004P P 20040514

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to aryl compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, m is 0-3; X, Y, and Z are independently selected from CH and N; L is (un)substituted (CH2)nO(CH2)n or (CH2)nS(O)p(CH2)n, where each n is independently selected from 0-4 and p is 0-2; R1 and R2 are independently selected from (un)substituted C3-12 cycloalkyl-A-, (un)substituted C3-8 heterocyclyl-A-, (un)substituted C6-10 aryl-A-, and (un)substituted C5-13 heteroaryl-A-, where A is a bond, C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; R3 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; and R4 is selected from (CH2)nO(CH2)nCO2R5 and (CH2)nCO2R5, where n is as defined previously and R5 is H or C1-6 alkyl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Substitution of Me bromoacetate with 4-hydroxy-3-methylacetophenone followed by Baeyer-Villiger oxidation and methanolysis gave phenoxyacetate II, which underwent substitution of 3,5-dibromobenzyl bromide to give dibromobenzyl ether III. Treatment of III with an excess of 4-trifluoromethylphenylboronic acid and ester hydrolysis resulted in the formation of terphenyl IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1259663 CAPLUS

DOCUMENT NUMBER: 144:22911

TITLE: Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Epple, Robert; Russo, Ross; Azimioara, Mihai; Xie, Yongping

PATENT ASSIGNEE(S): IRM LLC, Bermuda

SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113519	A1	20051201	WO 2005-US16672	20050512

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-571003P P 20040514

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to isoxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, R1 is selected from (un)substituted C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; R2 is selected from (CH2)nO(CH2)nOR5, (CH2)nOR5, CO2R5, C(O)N(R4)2, C(O)N(R4)(CH2)nOR4, CO2(CH2)nOR5, C(O)(CH2)nOR5, C(O)N(R4)(CH2)nOR5, C(O)N(R4)(R5), and C(O)N(R4)(CH2)nR5, where n is 0-4, R4 is H or C1-6 alkyl, and R5 is C1-6 alkyl, C3-12 cycloalkyl, C3-8 heterocyclyl, C6-10 aryl, or C5-10 heteroaryl, or R4 and R5, together with the nitrogen atom to which they are attached, form C3-8 heterocyclyl or C5-10 heteroaryl; and R3 is selected from (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Esterification of 3-bromophenylacetic acid followed by coupling with cyanide, reduction of the nitrile to an aldehyde, condensation with hydroxylamine, and chlorination gave chlorooxime II. N-Boc-2-bromoethylamine was substituted with 2,4-dichlorophenol followed by deprotection, amidation with Et benzoylacetate to give benzoylacetamide III, which underwent cyclocondensation with chlorooxime II and ester hydrolysis, resulting in the formation of isoxazole IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:57734 SCISEARCH

THE GENUINE ARTICLE: 997VR

TITLE: Protective effect of nonsteroidal anti-inflammatory drugs on colorectal adenomas is modified by a polymorphism in peroxisome proliferator-activated receptor delta

AUTHOR: Siezen C L E; Tijhuis M J; Kram N R; van Soest E M; de Jong D J; Fodde R; van Kranen H J; Kampman E (Reprint)

CORPORATE SOURCE: Univ Wageningen & Res Ctr, Div Human Nutr, Agrotechn, Bomenweg 2, Bode 62, NL-6703 HD Wageningen, Netherlands (Reprint); Univ Wageningen & Res Ctr, Div Human Nutr, Agrotechn, NL-6703 HD Wageningen, Netherlands; Erasmus Univ, Josephine Nefkens Inst, Dept Pathol, Rotterdam, Netherlands; Natl Inst Publ Hlth & Environm, Dept Toxicol Pathol & Genet, NL-3720 BA Bilthoven, Netherlands; Radboud Univ Nijmegen Med Ctr, Dept Gastroenterol & Hepatol, Nijmegen, Netherlands
Ellen.Kampman@wur.nl

COUNTRY OF AUTHOR: Netherlands

SOURCE: PHARMACOGENETICS AND GENOMICS, (JAN 2006) Vol. 16, No. 1, pp. 43-50.
ISSN: 1744-6872.

PUBLISHER: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3261 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 27
ENTRY DATE: Entered STN: 19 Jan 2006
Last Updated on STN: 26 Jan 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective Nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with a decreased risk of colorectal tumors. Single nucleotide polymorphisms (SNPs) in target genes of NSAID action, and their haplotypes, might modulate this protective effect. Methods A case-control study including 724 cases and 682 controls was used to evaluate the effect of NSAIDs on colorectal adenoma risk in The Netherlands, a country in which NSAID use is relatively low. Cases and controls were classified according to presence or absence of endoscopyproven, pathology-confirmed colorectal adenomas, ever in their lives. Thirteen SNPs in four genes (PPAR delta, PPAR gamma, PTGS1 and PTGS2) were genotyped in 787 subjects (384 cases and 403 controls). Results Compared to non-regular users (< 12 times/year), regular users of NSAIDs (>= 12 times/year) had a lower risk of colorectal adenomas (odds ratio (OR): 0.75, 95% confidence interval (Cl): 0.56-0.99). The results were similar for aspirin only. We found an interaction between SNP c. - 789C > T in **PPAR sigma** and NSAID use (P=0.03). The protective effect of NSAIDs was strengthened for regular users with the PPAR delta CT or TT genotypes (OR: 0.35, 95%Cl: 0.11-1.13), whereas a positive association was observed for non-regular users with these genotypes (OR: 2.24, 95%Cl: 1.06-4.73) as compared to non-regular users

with the CC genotype. Also, a statistically significant interaction between a major haplotype containing the minor allele of this SNP and NSAID use was observed. Conclusions This study confirms the protective effect of NSAIDs and suggests a modulating effect of a SNP in the promoter of PPAR delta. Pharmacogenetics and Genomics 16:43-50. (c) 2006 Lippincott Williams & Wilkins.

=> d L2

L2 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:607904 BIOSIS
DN PREV200200607904
TI Peroxisome proliferator activated receptors and the regulation of mammalian fatty acid metabolism.
AU Smith, S. A. [Reprint author]
CS GlaxoSmithKline, Harlow, Essex, CM19 5AW, UK
SO Biochemical Society Transactions, (2002) Vol. 30, No. 5, pp. A103. print.
Meeting Info.: Biochemical Society 677th Meeting. Wales, Cardiff, UK. December 07-10, 2002.
CODEN: BCSTB5. ISSN: 0300-5127.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

=> d L2 1-14 ibib,abs

L2 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:607904 BIOSIS
DOCUMENT NUMBER: PREV200200607904
TITLE: Peroxisome proliferator activated receptors and the regulation of mammalian fatty acid metabolism.
AUTHOR(S): Smith, S. A. [Reprint author]
CORPORATE SOURCE: GlaxoSmithKline, Harlow, Essex, CM19 5AW, UK
SOURCE: Biochemical Society Transactions, (2002) Vol. 30, No. 5, pp. A103. print.
Meeting Info.: Biochemical Society 677th Meeting. Wales,

Cardiff, UK. December 07-10, 2002.
CODEN: BCSTB5. ISSN: 0300-5127.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

L2 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:363775 BIOSIS
DOCUMENT NUMBER: PREV200200363775
TITLE: Peroxisome proliferator-activated receptors modulate K-Ras-mediated transformation of intestinal epithelial cells.
AUTHOR(S): Shao, Jinyi; Sheng, Hongmiao; DuBois, Raymond N. [Reprint author]
CORPORATE SOURCE: Department of Medicine/GI, Vanderbilt University Medical Center, MCN C-2104, Nashville, TN, 37232-2279, USA
raymond.dubois@mcmail.vanderbilt.edu
SOURCE: Cancer Research, (June 11, 2002) Vol. 62, No. 11, pp. 3282-3288. print.
CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jul 2002
Last Updated on STN: 3 Jul 2002
AB Activation of peroxisome proliferator-activated receptors (PPARs) exerts diverse effects on neoplastic cells. Recent work has shown that PPARdelta is up-regulated after loss of adenomatous polyposis coli tumor suppressor gene function and that transcriptional activation of the PPARgamma nuclear receptor can lead to inhibition of carcinoma growth. In this study, we elucidate the regulation and functional importance of PPARgamma and delta after K-Ras-transformation of intestinal epithelial cells. In conditionally K-Ras-transformed rat intestinal epithelial cells (IEC-iK-Ras), the level and activity of PPARdelta were markedly increased. PPARdelta up-regulation occurred due to increased mitogen-activated protein kinase activity and receptor activation required the endogenous production of prostacyclin via the cyclooxygenase-2 pathway. We also demonstrate that activation of the PPARgamma nuclear receptor has antineoplastic effects in Ras-transformed cells. Activation of PPARgamma resulted in a delay in transit through the G1 phase of the cell cycle that was associated with inhibition of phosphatidylinositol 3'-kinase/Akt activity and a reduction of cyclin D1 expression. Therefore, these two PPAR nuclear receptors, which are structurally related, have distinct roles during neoplastic transformation. PPARgamma appears to modulate differentiation and signal growth inhibition, whereas PPARdelta is up-regulated by oncogenic Ras and activated by cyclooxygenase-2-derived prostaglandins.

L2 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:149965 BIOSIS
DOCUMENT NUMBER: PREV200200149965
TITLE: Prostacyclin-dependent apoptosis mediated by PPARdelta.
AUTHOR(S): Hatae, Toshihisa; Wada, Masayuki; Yokoyama, Chieko; Shimonishi, Manabu; Tanabe, Tadashi [Reprint author]
CORPORATE SOURCE: Department of Pharmacology, National Cardiovascular Center Research Institute, Fujishiro-dai, Suita, Osaka, 565-8565, Japan
tanabe@jsc.ri.ncvc.go.jp
SOURCE: Journal of Biological Chemistry, (December 7, 2001) Vol. 276, No. 49, pp. 46260-46267. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002
AB Prostacyclin (PGI2) plays important roles in hemostasis both as a vasodilator and an endogenous inhibitor of platelet aggregation. PGI2

functions in these roles through a specific IP receptor, a G protein-coupled receptor linked to Gs and increases in cAMP. Here, we report that intracellular prostacyclin formed by expressing prostacyclin synthase in human embryonic kidney 293 cells promotes apoptosis by activating endogenous peroxisome proliferator-activated receptor delta (PPARdelta). In contrast, treatment of cells with extracellular prostacyclin or dibutyryl cAMP actually reduced apoptosis. On the contrary, treatment of the cells with RpcAMP (adenosine 3',5'-cyclic monophosphothioate, Rp-isomer), an antagonist of cAMP, enhanced prostacyclin-mediated apoptosis. The expression of an L431A/G434A mutant of PPARdelta completely blocked prostacyclin-mediated PPARdelta activation and apoptosis. These observations indicate that prostacyclin can act through endogenous PPARdelta as a second signaling pathway that controls cell fate.

L2 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:527101 BIOSIS
DOCUMENT NUMBER: PREV200100527101
TITLE: Expression and localization of PPARs in the rat ovary during follicular development and the periovulatory period.
AUTHOR(S): Komar, Carolyn M. [Reprint author]; Braissant, Olivier; Wahli, Walter; Curry, Thomas E., Jr.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Chandler Medical Center, University of Kentucky, 800 Rose Street, Room MS 331, Lexington, KY, 40536-0298, USA
ckomar@uky.edu
SOURCE: Endocrinology, (November, 2001) Vol. 142, No. 11, pp. 4831-4838. print.
CODEN: ENDOAO. ISSN: 0013-7227.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 2001
Last Updated on STN: 23 Feb 2002

AB PPARs are a family of nuclear hormone receptors involved in various processes that could influence ovarian function. We investigated the cellular localization and expression of PPARs during follicular development in ovarian tissue collected from rats 0, 6, 12, 24, and 48 h post-PMSG. A second group of animals received human CG (hCG) 48 h post-PMSG. Their ovaries were removed 0, 4, 8, 12, and 24 h post-hCG to study the periovulatory period. mRNAs corresponding to the PPAR isotypes (alpha, delta, and gamma) were localized by in situ hybridization. Changes in the levels of mRNA for the PPARs were determined by ribonuclease protection assays. PPARgamma mRNA was localized primarily to granulosa cells, and levels of expression did not change during follicular development. Four hours post-hCG, levels of mRNA for PPARgamma decreased ($P < 0.05$) but not uniformly in all follicles. At 24 h post-hCG, levels of PPARgamma mRNA were reduced 64%, but some follicles maintained high expression. In contrast, mRNAs for PPARalpha and delta were located primarily in theca and stroma, and their levels did not change during the intervals studied. To investigate the physiologic significance of PPARgamma in the ovary, granulosa cells from PMSG-primed rats were cultured for 48 h with prostaglandin J2 (PGJ2) and ciglitazone, PPARgamma activators. Both compounds increased progesterone and E2 secretion ($P < 0.05$). These data suggest that PPARgamma is involved in follicular development, has a negative influence on the luteinization of granulosa cells, and/or regulates the periovulatory shift in steroid production. The more general and steady expression of PPARs alpha and delta indicate that they may play a role in basal ovarian function.

L2 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:354368 BIOSIS
DOCUMENT NUMBER: PREV200000354368
TITLE: Adipose tissue development and redundancy.
AUTHOR(S): Ailhaud, G. [Reprint author]
CORPORATE SOURCE: Biologie du Developpement et Cancer, Laboratoire "Biologie du Developpement du Tissu Adipeux", Faculte des Sciences, Institut de Recherches Signalisation, Centre de Biochimie (UMR 6543 CNRS), UNSA, Parc Valrose, 06108, Nice Cedex 2,

France
SOURCE: International Journal of Obesity, (May, 2000) Vol. 24, No. Supplement 1, pp. S9. print.
Meeting Info.: 10th European Congress on Obesity of the European Association for the Study of Obesity. Antwerp, Belgium. May 24-27, 2000. European Association for the Study of Obesity.
CODEN: IJOBDP. ISSN: 0307-0565.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2000
Last Updated on STN: 8 Jan 2002

L2 ANSWER 6 OF 14 CABA COPYRIGHT 2006 CABI on STN
ACCESSION NUMBER: 2006:30027 CABA
DOCUMENT NUMBER: 20053221373
TITLE: Promising new targets for the next generation of anti-obesity drugs
AUTHOR: Cawthorne, M. A.; Antel, J. [EDITOR]; Finer, N. [EDITOR]; Heal, D. [EDITOR]; Krause, G. [EDITOR]
CORPORATE SOURCE: Clore Laboratory, University of Buckingham, Buckingham, MK18 1EG, UK.
SOURCE: Obesity and metabolic disorders. Fourth Solvay Pharmaceuticals Conference, Venice, Italy, 5-6 October 2003, (2005) pp. 201-213. 82 ref.
Publisher: IOS Press. Amsterdam
Price: Book chapter; Conference paper
Meeting Info.: Obesity and metabolic disorders. Fourth Solvay Pharmaceuticals Conference, Venice, Italy, 5-6 October 2003.
ISBN: 1-58603-535-5
PUB. COUNTRY: Netherlands Antilles
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 20060203
Last Updated on STN: 20060203

AB The market potential of an effective treatment for obesity is enormous, with millions of prospective patients worldwide. Thus far, anti-obesity treatments have been developed mainly from clinical observation of their effects, rather than by logical design. However, as illustrated by the extensive range of potential drug targets that has been discussed by various contributors to this book, it is almost certain that the next generation of drugs to treat obesity will enter clinical development via a more direct route. Patients, regulators and physicians have high expectations of anti-obesity drugs, and in the case of patients, these expectations are often unrealistic. Setting anticipation at a realistic level will be an educational challenge for the whole spectrum of healthcare providers, "opinion leaders", physicians and the pharmaceutical industry. Ideally, novel anti-obesity drugs should provide sustained weight loss, mainly of fat and not lean tissue; not only that, but fat loss should be from the abdominal cavity because this adipose depot carries the greatest risk for cardiovascular and metabolic complications. New anti-obesity drugs will need to have very favourable side effect and adverse event profiles. There must also be no tolerance to their pharmacological effect because drug therapy for obesity will inevitably be long-term. In addition to the extensive number of targets, which have been described and reviewed by the other authors of this book, there are many more that have not been discussed. Other potential molecular targets for developing novel anti-obesity drugs include the peroxisome-proliferator-activated receptors (**PPAR[sigma]** and PPAR[alpha]), the cannabinoid, oleylethanolamide, uncoupling proteins, 11[beta]-hydroxysteroid dehydrogenase, the neuropeptide-Y5 receptor, ghrelin, the galanin-1 receptor and the melanocortin-4 receptor.

L2 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1262399 CAPLUS
DOCUMENT NUMBER: 144:22712

TITLE: Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Epple, Robert; Azimioara, Mihai
PATENT ASSIGNEE(S): Irm LLC, Bermuda
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113506	A1	20051201	WO 2005-US16747	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-571004P P 20040514
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to aryl compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, m is 0-3; X, Y, and Z are independently selected from CH and N; L is (un)substituted (CH2)nO(CH2)n or (CH2)nS(O)p(CH2)n, where each n is independently selected from 0-4 and p is 0-2; R1 and R2 are independently selected from (un)substituted C3-12 cycloalkyl-A-, (un)substituted C3-8 heterocyclyl-A-, (un)substituted C6-10 aryl-A-, and (un)substituted C5-13 heteroaryl-A-, where A is a bond, C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; R3 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; and R4 is selected from (CH2)nO(CH2)nCO2R5 and (CH2)nCO2R5, where n is as defined previously and R5 is H or C1-6 alkyl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Substitution of Me bromoacetate with 4-hydroxy-3-methylacetophenone followed by Baeyer-Villiger oxidation and methanolysis gave phenoxyacetate II, which underwent substitution of 3,5-dibromobenzyl bromide to give dibromobenzyl ether III. Treatment of III with an excess of 4-trifluoromethylphenylboronic acid and ester hydrolysis resulted in the formation of terphenyl IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1259663 CAPLUS

DOCUMENT NUMBER: 144:22911
TITLE: Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Epple, Robert; Russo, Ross; Azimioara, Mihai; Xie, Yongping
PATENT ASSIGNEE(S): IRM LLC, Bermuda
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113519	A1	20051201	WO 2005-US16672	20050512

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-571003P P 20040514
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to isoxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, R1 is selected from (un)substituted C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; R2 is selected from (CH2)nO(CH2)nOR5, (CH2)nOR5, CO2R5, C(O)N(R4)2, C(O)N(R4)(CH2)nOR4, CO2(CH2)nOR5, C(O)(CH2)nOR5, C(O)N(R4)(CH2)nOR5, C(O)N(R4)(R5), and C(O)N(R4)(CH2)nR5, where n is 0-4, R4 is H or C1-6 alkyl, and R5 is C1-6 alkyl, C3-12 cycloalkyl, C3-8 heterocyclyl, C6-10 aryl, or C5-10 heteroaryl, or R4 and R5, together with the nitrogen atom to which they are attached, form C3-8 heterocyclyl or C5-10 heteroaryl; and R3 is selected from (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Esterification of 3-bromophenylacetic acid followed by coupling with cyanide, reduction of the nitrile to an aldehyde, condensation with hydroxylamine, and chlorination gave chlorooxime II. N-Boc-2-bromoethylamine was substituted with 2,4-dichlorophenol followed by deprotection, amidation with Et benzoylacetate to give benzoylacetamide III, which underwent cyclocondensation with chlorooxime II and ester hydrolysis, resulting in the formation of isoxazole IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

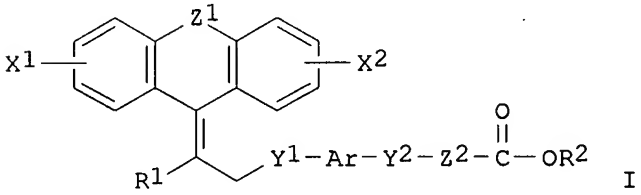
L2 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1193301 CAPLUS
DOCUMENT NUMBER: 143:459875
TITLE: Preparation of substituted phenoxyacetic acids as peroxisome proliferator-activated receptor ligands
INVENTOR(S): Polivka, Zdenek
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105736	A1	20051110	WO 2005-EP52013	20050503

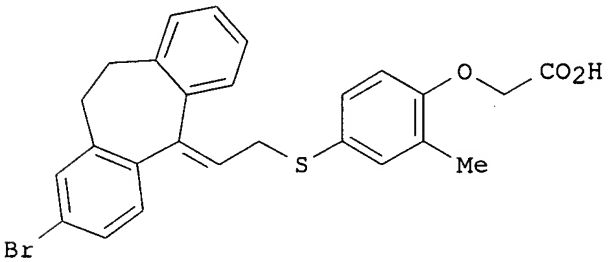
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2004-718 A 20040505
GI



I



II

AB Title compds. I [X1-2 = H, halo, OH, CN, etc.; Ar = (un)substituted arylene; Y1-2 = O, S; Z1 = (CH2)0-3; Z2 = (CH2)1-3; R1 = H, halo, alkyl, etc.; R2 = H, (cyclo)alkyl, alkenyl, etc.] are prepared For instance, II is prepared in 9 steps from 3-bromotoluene, phthalaldehydic acid and [(4-mercapto-2-methylphenyl)oxy]acetic acid Et ester. I are peroxisome proliferator-activated receptor (PPARδ) agonists [no data] and are useful for the treatment of, e.g., diabetes.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:45929 CAPLUS

DOCUMENT NUMBER: 128:215738
TITLE: Structural requirements and cell-type specificity for ligand activation of peroxisome proliferator-activated receptors
AUTHOR(S): Johnson, Timothy E.; Holloway, M. Katharine; Vogel, Robert; Rutledge, Sue Jane; Perkins, James J.; Rodan, Gideon A.; Schmidt, Azriel
CORPORATE SOURCE: Department of Genetic and Cellular Toxicology, Merck and Company, West Point, PA, 19486, USA
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1997), 63(1-3), 1-8
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mammalian peroxisome proliferator-activated receptor (PPAR) family consists of three different subtypes, PPARα, hNUC1/ **PPAR**. **sigma**. and PPARγ. Selective agonists have been identified for PPARα and PPARγ but not for hNUC1, and consequently little is known about the genes that are controlled by this receptor. Using ligand-dependent transcription assays in COS-7 cells, we screened a variety of PPAR activating agents to identify a selective activator of hNUC1. We found that the potent peroxisome proliferator, Wy-14643, and the PPARγ-selective thiazolidinedione, BRL 49653, were poor activators of hNUC1 (EC50s of >100 μM). Short chain fatty acids (FAs) appeared more selective for PPARα than for hNUC1, whereas the very long chain FA, erucic acid (C22:1) was more selective for hNUC1. Using erucic acid as a probe, we conducted a topol. similarity search of the Merck Chemical Collection and identified a fatty acid-like compound, L-631,033 4-(2-acetyl-6-hydroxyundecyl) cinnamic acid, that was a selective activator of hNUC1 (EC50 of 2 μM), but was much less selective for PPARα or PPARγ (EC50s of >100 μM). Structure-function anal. of PPAR activation by L-631,033 structural analogs showed that receptor selectivity depends on the position of the carboxyl group relative to the Ph ring on the mol. Transfection expts. in several cell types: an osteoblastic cell line (MB 1.8), a mouse liver cell line (ML-457), rat aortic smooth muscle cells (RSMCs) and COS-7 cells revealed differences in the activation profile of specific ligands. The most notable differences were observed in RSMCs, where transactivation by L-631,033 and Wy-14643, but not by BRL 49653, was markedly reduced, and in MB 1.8 cells, where oleic acid failed to activate PPARs. These findings identify certain structural features in PPAR-activating agents that modulate PPAR activation, and suggest that as with other nuclear receptors, activation is cell-type specific.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 14 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-29474 DRUGU P S
TITLE: New molecular bioassays in vitro for the estimation of the teratogenic potency of valproic acid-metabolites.
AUTHOR: Lampen A; Nau H; Ellerbeck U; Gottlicher M
LOCATION: Karlsruhe, Ger.
SOURCE: Arch.Pharmacol. (359, No. 3, Suppl., R161, 1999)
CODEN: NSAPCC ISSN: 0028-1298
AVAIL. OF DOC.: Zentrumsabteilung fur Lebensmitteltoxikologie, Tierarztliche Hochschule Hannover, Institut fur Genetik, Forschungszentrum Karlsruhe, Deutschland.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1999-29474 DRUGU P S

AB The Authors studied the structure-activity relationships of valproate (VPA) and its metabolites, 2-propyl-4-pentynoic acid (S-4-yn-VPA), 2-heptyl-4-pentynoic acid (heptyl-4-yn-VPA), 2-hexyl-4-pentynoic acid (hexyl-4-yn-acid), 2-pentyl-4-pentynoic acid (pentyl-4-yn-acid), 2-butyl-4-pentynoic acid (butyl-4-yn-acid) and 2-propyl-2-pentenoic acid

(4-en-VPA) in CHO cells stably expressing hybrid proteins of the ligand-binding domain of peroxisome proliferator-activated protein (PPAR) alpha, sigma and gamma. Results showed that no activity was present in with the alpha and gamma subtypes; however, data showed that **PPAR -sigma** may be a potential mediator of VPA-induced teratogenicity. (conference abstract: 40th Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology, Mainz, Germany, 1999). (No EX).
ABEX (KH)

L2 ANSWER 12 OF 14 JICST-EPlus COPYRIGHT 2006 JST on STN
ACCESSION NUMBER: 990473663 JICST-EPlus
TITLE: Molecular mechanism of gene expression of CRBP II and L-FABP with fluctuation of PPARA/ **PPAR**. **SIGMA**. ratio in intestinum tenue by high fat diet intake.
AUTHOR: MOCHIZUKI KAZUKI; SURUGA KAZUHITO; GODA TOSHIHISA; TAKASE SACHIKO
CORPORATE SOURCE: Shizuoka Prefectural Univ.
SOURCE: Nippon Eiyo, Shokuryo Gakkai Sokai Koen Yoshishu, (1999) vol. 53rd, pp. 218. Journal Code: X0098A
PUB. COUNTRY: Japan
DOCUMENT TYPE: Conference; Short Communication
LANGUAGE: Japanese
STATUS: New

L2 ANSWER 13 OF 14 LIFESCI COPYRIGHT 2006 CSA on STN
ACCESSION NUMBER: 96:80338 LIFESCI
TITLE: Differential activation of adipogenesis by multiple PPAR isoforms
AUTHOR: Brun, R.P.; Tontonoz, P.; Forman, B.M.; Ellis, R.; Chen, J.; Evans, R.M.; Spiegelman, B.M.*
CORPORATE SOURCE: Dana-Farber Cancer Inst. and Dep. Cell Biol., Harvard Med. Sch., Boston, MA 02115, USA
SOURCE: GENES DEV., (1996) vol. 10, no. 8, pp. 974-984. ISSN: 0890-9369.
DOCUMENT TYPE: Journal
FILE SEGMENT: N
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Peroxisome proliferator-activated receptor gamma (PPAR gamma) is a nuclear hormone receptor expressed predominantly in adipose tissue, where it plays a central role in the control of adipocyte gene expression and differentiation. Because there are two additional PPAR isoforms, PPAR alpha and PPAR delta , and these are also expressed at some level in certain adipose depots, we have compared directly the adipogenic potential of all three receptors. Ectopically expressed PPAR gamma powerfully induces adipogenesis at a morphological and molecular level in response to a number of PPAR gamma activators. PPAR gamma is less adipogenic but is able to induce significant differentiation in response to strong PPAR gamma activators. Expression and activation of **PPAR sigma** did not stimulate adipogenesis. Of the three PPARs, only PPAR gamma can cooperate with C/EBP alpha in the promotion of adipogenesis. To begin to investigate the functional basis for the differential adipogenic activity of the PPAR isoforms, we have examined their ability to bind to several PPAR DNA response sequences. Compared with PPAR alpha and PPAR delta , PPAR gamma shows preferential binding to two well-characterized regulatory sequences derived from a fat-specific gene, ARE6 and ARE7. These data strongly suggest that PPA gamma is the predominant receptor regulating adipogenesis; however, they also suggest that PPAR alpha may play a role in differentiation of certain adipose depots in response to a different set of physiologic activators or in certain disease states.

L2 ANSWER 14 OF 14 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:57734 SCISEARCH
THE GENUINE ARTICLE: 997VR

TITLE: Protective effect of nonsteroidal anti-inflammatory drugs on colorectal adenomas is modified by a polymorphism in peroxisome proliferator-activated receptor delta

AUTHOR: Siezen C L E; Tijhuis M J; Kram N R; van Soest E M; de Jong D J; Fodde R; van Kranen H J; Kampman E (Reprint)

CORPORATE SOURCE: Univ Wageningen & Res Ctr, Div Human Nutr, Agrotechn, Bomenweg 2, Bode 62, NL-6703 HD Wageningen, Netherlands (Reprint); Univ Wageningen & Res Ctr, Div Human Nutr, Agrotechn, NL-6703 HD Wageningen, Netherlands; Erasmus Univ, Josephine Nefkens Inst, Dept Pathol, Rotterdam, Netherlands; Natl Inst Publ Hlth & Environm, Dept Toxicol Pathol & Genet, NL-3720 BA Bilthoven, Netherlands; Radboud Univ Nijmegen Med Ctr, Dept Gastroenterol & Hepatol, Nijmegen, Netherlands
Ellen.Kampman@wur.nl

COUNTRY OF AUTHOR: Netherlands

SOURCE: PHARMACOGENETICS AND GENOMICS, (JAN 2006) Vol. 16, No. 1, pp. 43-50.
ISSN: 1744-6872.

PUBLISHER: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3261 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 27

ENTRY DATE: Entered STN: 19 Jan 2006
Last Updated on STN: 26 Jan 2006

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective Nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with a decreased risk of colorectal tumors. Single nucleotide polymorphisms (SNPs) in target genes of NSAID action, and their haplotypes, might modulate this protective effect. Methods A case-control study including 724 cases and 682 controls was used to evaluate the effect of NSAIDs on colorectal adenoma risk in The Netherlands, a country in which NSAID use is relatively low. Cases and controls were classified according to presence or absence of endoscopyproven, pathology-confirmed colorectal adenomas, ever in their lives. Thirteen SNPs in four genes (PPAR delta, PPAR gamma, PTGS1 and PTGS2) were genotyped in 787 subjects (384 cases and 403 controls). Results Compared to non-regular users (< 12 times/year), regular users of NSAIDs (>= 12 times/year) had a lower risk of colorectal adenomas (odds ratio (OR): 0.75, 95% confidence interval (Cl): 0.56-0.99). The results were similar for aspirin only. We found an interaction between SNP c. - 789C > T in **PPAR sigma** and NSAID use (P=0.03). The protective effect of NSAIDs was strengthened for regular users with the PPAR delta CT or TT genotypes (OR: 0.35, 95%Cl: 0.11-1.13), whereas a positive association was observed for non-regular users with these genotypes (OR: 2.24, 95%Cl: 1.06-4.73) as compared to non-regular users

with the CC genotype. Also, a statistically significant interaction between a major haplotype containing the minor allele of this SNP and NSAID use was observed. Conclusions This study confirms the protective effect of NSAIDs and suggests a modulating effect of a SNP in the promoter of PPAR delta. Pharmacogenetics and Genomics 16:43-50. (c) 2006 Lippincott Williams & Wilkins.